REMARKS

New claims 23 and 24 are submitted as the restriction requirement appeared to be an election of species. Accordingly, it is believed claim 23 is proper as additional species may be examined in the same application. Claim 24 is a method of use of the compositions of the previous claims, and if the composition claims are allowable, should be examined along with them.

The claims have been amended to expedite prosecution by mooting an issue raised by the Office under 35 U.S.C. § 112, paragraph 1. Claim 7 has been amended to be limited to peptides containing epitope sequences that have been demonstrated to elicit an immunologic response. The peptides now included are also believed to be novel. The one peptide on the list which was indicated disclosed in the art has been deleted, and applicants are unable to find prior art disclosing those now claimed. Claim 17 has been clarified to indicate that the peptide of 15 amino acids or less is linked to another peptide that is a T helper epitope. The amendments to the claims appear to applicants to dispose of the outstanding issues in light of the discussion to follow.

Evidence of Immunogenicity

The peptides now claimed have been described in refereed publications as meeting recognized tests for immunogenicity or demonstrated as immunogenic by declaration.

Several members of the class of peptides now claimed were tested for immunogenicity in an article by Keogh, E., *et al., J. Immunol.* (2001) 167:787-796. Table II on page 791 shows the results of several analogs derived from p53 which are presented in the present application as SEQ. ID. NOs: 4, 5, 8 and 9. The analysis for immunogenicity was an *in vitro* assay wherein peptide loaded dendrocytes were tested for their capacity to induce responses in target cells. The

target cells were of the .221A2 cell line which is produced by transferring the HLA-A2.1 gene into a null B lymphoblastoid cell line .221 which lacks HLA-A, B and C alleles. As shown in Table II, taken in the order in which they appear in the table, SEQ. ID. NO: 8 (p53.129B7V9, #12) induced positive responses in two of four CTL inductions when the CTL's were pulsed with the peptide; SEQ. ID. NO: 9 (p53.139L2B3, #18) induced positive results in three of four reactions; SEQ. ID. NO: 4 (p53.149M2, #20) induced positive reactions in two of four experiments; and SEQ. ID. NO: 5 (p53.149L2, #21) induced positive responses in two of three. Part of the point of the paper was to ascertain the ability of the analogs to elicit a cellular immune response with respect to both wildtype peptide and to SEQ. ID. NOs: 4, 5 and 9 succeeded in this regard. Extensive data for SEQ. ID. NO: 5 are also presented in Petersen, T.R., *Scand. J. Immunol.* (2001) 53:357-364; See Table 1, #2, Figure 2A and 3A.

Also presented in the Keogh paper are results for sequences derived directly from, or analogous to, Her2/*neu* peptides and the results for SEQ. ID. NOs: 188 and 191 are shown in Table III on page 793. As shown, in the order set forth in the table. SEQ. ID. NO: 188 (Her2/*neu*.665L2V9, #5) successfully induced a positive response in four of four target cell lines pulsed with the peptide itself and two of four cell lines pulsed with wildtype corresponding peptide; SEQ. ID. NO: 191 (Her2/*neu*.952L2B7V10,#7) induced positive results in three of three reactions using peptide-pulsed target cell line.

The Keogh paper also provides results for the CEA-derived antigens, SEQ. ID. NO: 33 and SEQ. ID. NO: 3, in Table V on page 794 and Table II on p.793 respectively. As shown, SEQ. ID. NO: 33 (CEA.687,#1 in Table V) was successful in eliciting positive results. SEQ. ID. NO: 3 (CEA 605V9, #6 in Table II) also elicited positive results. The other claimed CEA-

derived anitgen, SEQ. ID. NO: 31, is shown immunogenic by the enclosed technical report authenticated by the declaration of Scott Southwood.

Peptides of SEQ. ID. NOs: 182, 183 and 184 were tested for immunogenicity and the results reported in Gianfrani, C., *et al., Human Immunology* (2000) 61:438-452. The tests were based on determination of binding to purified MHC, immunization of transgenic mice containing the appropriate allele, and determination of recall CTL responses using PBMC from the appropriately typed individuals. The results are shown, for example, with regard to the tests run in transgenic mice in Table 1 on page 441. As indicated in the table, the peptide of SEQ. ID. NO: 182 (pa46, #1), SEQ. ID. NO: 184 (pa225,#13), and SEQ. ID. NO: 183 (pb1.413,#3) all showed positive results in significant numbers of mice. (The peptides are listed in the order in which they appear in the table.)

Attached hereto as Exhibit B is a chart summarizing the locations of evidence for these positive results.

The Rejections

Formal Matters

It is believed that the claims as now presented are in conformance with applicants election. The claims all relate to the same invention, but claims not considered were withdrawn from consideration as a result of an election of species. Only alternative species of the same invention are presented, with the possible exception of claim 24 which is a modified form of former claims 2-6. According to MPEP § 821.04 and the Official Gazette Notice 1184 OG 86. (1996), should claims to compositions be allowable, methods of using the compositions should be rejoined with the composition claims and examined in the same application.

Applicants wish to defer correction of the abstract pending the outcome of the examination of the proposed claims.

The objection to the specification has been addressed by amendment. Priority to an earlier application is no longer being claimed.

The Rejection Under 35 U.S.C. § 112, First Paragraph

The pending claims were rejected as not enabled by the specification because the specification is said to contain no evidence that the claimed peptides are actually immunogenic. While applicants do not agree with the position taken by the Office that there is a necessity for data in the specification to establish immunogenicity, applicants have confined the claims to peptides for which immunogenicity has been established. The details of establishing this immunogenicity are set forth hereinabove. Accordingly, it is believed that this basis for rejection is moot.

The Rejection Over the Art

The peptide which is said to destroy novelty of the claims in which it is included has been deleted from the claims. As the Examiner has acknowledged, claim 11 as previously pending, and as pending now, is free of the art. It is believed that all of the peptides now included in the claims are free of the art as well. Accordingly, this basis for rejection may be withdrawn.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 17 was considered unclear because the peptide that would result from linking the claimed immunogenic peptide to another peptide would exceed 15 amino acids. Of course it will. But the only peptide that is limited to 15 amino acids is that which is itself linked to an additional peptide. It is believed that the amendment to claim 17 clarifies this.

CONCLUSION

The claims have been amended to include only peptides for which evidence of immunogenicity has been submitted and which are free of the prior art. Accordingly, it is believed that the pending claims, claims 7-12, 14 and 16-24 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 399632001920.

Respectfully submitted,

Dated: January 18, 2002

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

7. (Amended) A composition comprising an immunogenic peptide of less than about 15 amino acids in length that comprises an HLA-A2.1 binding motif, wherein the immunogenic peptide comprises a sequence selected from the group consisting of [SEQ. ID. NOs: 1-217] :

YLSGANLNV (SEQ. ID. NO: 3),
SMPPPGTRV (SEQ. ID. NO: 4),
SLPPPGTRV (SEQ. ID. NO: 5),
ALNKMFBQV (SEQ. ID. NO: 8),
KLBPVQLWV (SEQ. ID. NO: 9),
YVCGIQNSV (SEQ. ID. NO: 31),
ATVGIMIGV (SEQ. ID. NO: 33),
FMYSDFHFI (SEQ. ID. NO: 182),
NMLSTVLGV (SEQ. ID. NO: 183),
SLENFRAYV (SEQ. ID. NO: 184),
VLLGVVFGV (SEQ. ID. NO: 188), and
YLIMVKBWMV (SEQ. ID. NO: 191).

8. (Amended) The composition of claim 7, wherein the sequence is from a cancer-associated antigen and is selected from the group consisting of [SEQ ID NOs: 1-43, 99, 170-175, 179, 180, 185-197, and 199-217] SEQ. ID. NOs: 3-5, 8, 9, 31, 33, 188, and 191.

9. (Amended) The composition of claim 8, wherein the cancer-associated antigen is p53 and the sequence is selected from the group consisting of [SEQ ID NOs: 4-17, 20-28, 37-43, and 196] SEQ. ID. NOs: 4, 5, 8, and 9.

11. (Amended) The composition of claim [10] 9, wherein the sequence is SEQ ID NO: 4.

12. (Amended) The composition of claim 8, wherein the cancer-associated antigen is carcinoembryonic antigen (CEA) and the peptide is selected from the group consisting of [SEQ. ID. NOs: 2, 3, 29-36, 99170-175, 179, 194, and 195] SEQ. ID. NOs: 31 and 33.

14. (Amended) The composition of claim 8, wherein the cancer-associated antigen is Her2/neu and the peptide is [selected from the group consisting of SEQ. ID. NOs: 180, 187-] SEQ. ID. NO: 188 or 191[, and 199].

17. (Amended) The composition of claim 7, wherein the immunogenic peptide of less than about 15 amino acids in length that comprises the HLA-A2.1 binding motif is linked to a T helper peptide.

EXHIBIT B. - LOCATIONS OF EVIDENCE FOR POSITIVE RESULTS

SEQ ID	Sequence	Source	Results
3	YLSGANLNV	CEA	Keogh, Table II, #6
4	SMPPPGTRV	p53	Keogh Table II, #20
5	SLPPPGTRV	p53	Keogh Table II, #21, Petersen, Table 1,#2,Fig.2A, Fig. 3A
8	ALNKMFBQV	p53	Keogh Table II, #12
9	KLBPVQLWV	p53	Keogh Table II, #18
31	YVCGIQNSV	CEA	Declaration of Scott Southwood
33	ATVGIMIGV	CEA	Keogh Table V, #1
182	FMYSDFHFI	Flu	Gianfrani Table 1, #1
183	NMLSTVLGV	Flu	Gianfrani Table 1, #13
184	SLENFRAYV	Flu	Gianfrani Table 1, #3
188	VLLGVVFGV	Her2	Keogh Table III, #5
191	YLIMVKBWMV	Her2	Keogh Table III, #7